

Claims 1-11 are pending.

Claims 1-11 have been rejected under 35 USC 103(a) as being allegedly unpatentable over Turner (J. Med Chem.) and Ehrfeld. This rejection is traversed.

Turner et al. discloses the synthesis of TPV. According to scheme 1 on page 3468 and the experimental section on page 3472 the intermediate 5,6-dihydro-4-hydroxy-6-phenethyl-6-propyl-2H-pyran-2-one is obtained by reacting in a first step metalated methylacetoacetate (via reaction with sodium hydride) with 1-phenyl-3-hexanone in the presence of n-BuLi. The reaction mixture is poured into aqueous NH₄Cl and rendered acidic. The reaction product is purified by extraction with EtOAc and washing of the organic phase with brine and drying with MgSO₄ and removal of the solvent. In a second step the intermediate is obtained by cyclization of the purified reaction product in the presence of a base.

W. Ehrfeld et al. describe the mixing quality of a single mixing unit and mixer arrays having various designs. For the characterization a fast inorganic reaction was employed wherein the iodine concentration was detected by UV-vis spectroscopy. In the introductory part of the article the authors very generally state a great potential of such mixers.

Ehrfeld's et al. article however does not teach or suggest that such micromixers are advantageously suitable for preparing dihydropyrones according to the general formula (I). Neither is the requisite motivation provided by Ehrfeld et al. to modify the teaching of Turner et al to arrive at the present invention. The reaction as described by Turner et al. starts with a slurry which is not suited to be employed in a micromixer as it would plug the narrow channels of the mixing elements. Furthermore a reaction time of 1 h at 0°C was specified by Turner et al.. Such long reaction times usually cannot be achieved in micromixers. The general advantage of micromixers is to carry out chemical reactions which demand a high heat flow, i.e. which otherwise would be too fast or even uncontrollable. In the present case one skilled in the art would not consider the reaction as presented by Turner et al. to be advantageously transferred to micromixers.

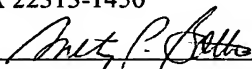
Surprisingly the inventors found that by carrying out the reaction according to the present invention a high yield of the product in a high purity can be obtained. According to the example 1 a yield of 92% was obtained although the reaction product of the first step was not purified but directly employed in the second step. Even variations of the reaction conditions resulted in high yields between 82 and 88%. Based on the volume flow and the size and length of the capillary a residence time of the reaction mixture of about or less than 1 min. is achieved. Against this background it is surprising that yields were obtained which are considerably higher than 72% as obtained by Turner et al..

In view of the foregoing withdrawal of the rejection is respectfully requested.

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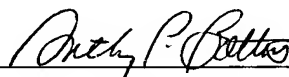
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